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Registration Decision RD2012-14

Penthiopyrad

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Registration Decision for Penthiopyrad

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting full registration for the sale and use of Penthiopyrad Technical Fungicide, Fontelis Fungicide, Vertisan Fungicide, Treoris Fungicide and DPX-LEM17 50WG Fungicide, containing the technical grade active ingredient penthiopyrad, to control or suppress various fungal diseases on a broad range of agricultural crops and turfgrass.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

These products were first proposed for registration in the consultation document[1] Proposed Registration Decision PRD2011-26, *Penthiopyrad*. This Registration Decision[2] describes this stage of the PMRA's regulatory process for penthiopyrad and summarizes the Agency's decision, the reasons for it and provides, in Appendix I, a summary of comments received during the consultation process as well as the PMRA's response to these comments. This decision is consistent with the proposed registration decision stated in PRD2011-26, with the exception that the claim for sclerotinia stem rot (*Sclerotinia sclerotiorum*) will be amended from suppression to control on the Vertisan Fungicide label.

For more details on the information presented in this Registration Decision, please refer to the Proposed Registration Decision PRD2011-26, *Penthiopyrad*, which contains a detailed evaluation of the information submitted in support of this registration.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[3] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions of registration. The Act also requires that products have value[4] when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

3 "Acceptable risks" as defined by subsection 2(2) of *Pest Control Products Act*.

4 "Value" as defined by subsection 2(1) of *Pest Control Products Act*"...the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact".

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

What Is Penthiopyrad?

Penthiopyrad is a systemic fungicide that can be applied to plant foliage or in-furrow to control or suppress various fungal diseases on a broad range of agricultural crops and turfgrass. This fungicide is a new active ingredient found in four end-use products, one of which is in combination with chlorothalonil (Treoris Fungicide).

Health Considerations

Can Approved Uses of Penthiopyrad Fungicide Affect Human Health?

Products containing penthiopyrad are unlikely to affect your health when used according to label directions.

Potential exposure to Penthiopyrad Technical Fungicide (referred to as penthiopyrad) may occur through the diet (food and water), when handling and applying the product or when entering treated sites. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when pesticide products are used according to label directions.

In laboratory animals, the acute toxicity of the active ingredient penthiopyrad was low via the oral, dermal and inhalation routes of exposure. Penthiopyrad was minimally irritating to the eyes, non-irritating to the skin and did not cause an allergic skin reaction.

The acute toxicity of the end-use product Vertisan Fungicide was low via the oral, dermal and inhalation routes of exposure. It was mildly irritating to the skin and severely irritating to the eyes; consequently, the hazard signal words "DANGER – EYE IRRITANT" and "SKIN IRRITANT" are required on the label. Vertisan Fungicide has the potential to cause allergic skin reactions; consequently, the hazard signal words "POTENTIAL SKIN SENSITIZER" are required on the label.

The acute toxicity of the end-use product Fontelis Fungicide was low via the oral, dermal and inhalation routes of exposure. It was non-irritating to the skin and minimally irritating to the eyes. Fontelis Fungicide is considered to have the potential to cause an allergic skin reaction; consequently, the hazard signal words "POTENTIAL SKIN SENSITIZER" are required on the label.

The acute toxicity of the end-use product Treoris Fungicide was low via the oral and dermal routes of exposure. It was slightly toxic via the inhalation route following acute exposure; consequently, the hazard signal words "CAUTION – POISON" are required on the label. Treoris Fungicide was mildly irritating to the skin, minimally irritating to the eyes and has the potential to cause allergic skin reactions; consequently, the hazard signal words "SKIN IRRITANT" and "POTENTIAL SKIN SENSITIZER" are required on the label.

The acute toxicity of the end-use product DPX-LEM17 50WG Fungicide was low via the oral, dermal and inhalation routes of exposure. It was slightly irritating to the skin, mildly irritating to the eyes and did not cause an allergic skin reaction; consequently, the hazard signal words "CAUTION – EYE IRRITANT" are required on the label.

Health effects in animals given repeated doses of penthiopyrad included changes in the liver, thyroid, adrenals and kidneys. Penthiopyrad did not cause birth defects in animals and there were no effects on the ability to reproduce. When penthiopyrad was given to pregnant or nursing animals, effects on the developing fetus and juvenile animal (reduced survival, pup and litter weights, body size, thymus weight, altered thymus development and/or delayed sexual development) were observed at doses that were toxic to the mother, indicating that the young do not appear to be more sensitive to penthiopyrad than the adult animal. Penthiopyrad caused temporary functional effects, possibly related to the nervous system, however, there was no indication that penthiopyrad caused damage to the nervous system. There was no evidence to suggest that penthiopyrad damaged genetic material. Penthiopyrad did, however, cause thyroid tumours in rats. There was also evidence of an effect on the immune system at high doses.

The risk assessment protects against the effects of penthiopyrad by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Aggregate dietary intake estimates (food plus water) revealed that the general population and infants, the subpopulation which would ingest the most penthiopyrad relative to body weight, are expected to be exposed to less than 19% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from penthiopyrad is not of concern for all population sub-groups. There were no cancer risks of concern.

An aggregate (food and water) dietary intake estimate for the highest exposed population (infants) was 6% of the acute reference dose, which is not a health concern.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Residue trials conducted throughout Canada and the United States using penthiopyrad on carrot, radish, sugar beet, potato, turnip, dry bulb onion, green onion, lettuce, spinach, celery, broccoli, cauliflower, cabbage, mustard green, pea, bean, soybean, tomato, pepper, cucumber, squash, cantaloupe, apple, pear, peach, plum, cherry, strawberry, almond, pecan, wheat, barley, sorghum, corn, canola, sunflower, cotton, peanut and alfalfa were acceptable. The MRLs for this active ingredient can be found in the Science Evaluation of PRD2011-26.

Occupational Risks From Handling Fontelis Fungicide, Vertisan Fungicide, Treoris Fungicide and DPX-LEM17 50WG Fungicide

Occupational risks are not of concern when products containing penthiopyrad are used according to the label directions, which include protective measures.

Farmers and custom applicators who mix, load or apply Fontelis Fungicide, Vertisan Fungicide, Treoris Fungicide and DPX-LEM17 50WG Fungicide, as well as field workers entering freshly treated fields and greenhouses, can come in direct contact with penthiopyrad residues on the skin. Therefore, the label specifies that anyone mixing/loading and applying products containing penthiopyrad must wear a long-sleeved shirt, long pants, shoes, socks and chemical resistant gloves while mixing/loading, applying and during clean-up and repair. In addition, when handling Vertisan Fungicide, goggles or a face shield are required during mixing/loading and during clean-up and repair. The label also requires that workers do not enter corn fields for three days after application for detasseling and for 12 hours after application for all other agricultural activities, or until sprays have dried for turf. Taking into consideration these label statements, the number of applications and the expectation of the exposure period, risk to handlers and workers is not a concern. There were no cancer risks of concern.

Risks in Residential and Other Non-Occupational Environments

Non-occupational risks are not of concern when Fontelis Fungicide and DPX-LEM17 50WG Fungicide are used according to label directions.

Adults and youth may be exposed to penthiopyrad while golfing on treated courses. Based on the expected short- to intermediate-term duration of this activity, risk to golfers is not a concern. Adults, youths and toddlers may be exposed to penthiopyrad when entering treated lawns or during pick-your-own harvesting activities. In addition, toddlers may have incidental oral exposure during hand-to-mouth activities or from ingesting treated grass or soil. Based on the expected short- to intermediate-term duration of these activities, risk to the general population is not of concern. There were no cancer risks of concern.

Environmental Considerations

What Happens When Penthiopyrad Is Introduced Into the Environment?

When applied as a foliar spray to control diseases on a variety of crops, penthiopyrad does not leach appreciably and is degraded rapidly on the soil surface. When applied in furrow, or if it leaches below the soil surface, penthiopyrad does not readily degrade. Penthiopyrad is not volatile and is not expected to bioaccumulate.

Penthiopyrad will be persistent in aquatic environments and can potentially affect aquatic life. Aquatic life stages of amphibians would potentially be at the highest risk through exposure from off-target spray drift and surface runoff entering aquatic systems. There is also a risk to freshwater invertebrates and fish and algae. The effects of penthiopyrad on aquatic ecosystems can be mitigated with the observance of precautionary measures, including spray drift buffer zones.

Value Considerations

What Is the Value of Fontelis Fungicide, Vertisan Fungicide, Treoris Fungicide and DPX-LEM17 50WG Fungicide?

Fontelis Fungicide is a suspension concentrate product for foliar and in-furrow uses on a broad range of crops, including cereals, fruit crops, vegetable crops and nuts.

Vertisan Fungicide is an emulsifiable concentrate for foliar and in-furrow application to field crops, including cereals, oilseeds, sugarbeets, legumes, and root and corm vegetables.

Treoris Fungicide is a pre-mix with chlorothalonil to control diseases on potatoes and cucurbits.

DPX-LEM17 50WG Fungicide is a water dispersible granule formulation to control turf diseases.

Penthiopyrad is a new mode of action fungicide for many crops that can be integrated into a spray program as a rotational product or tank mix partner. These products address primary diseases of major field crops as well as minor crops grown in Canada.

Measures to Minimize Risk

Registered pesticide product labels include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures on the label of Fontelis Fungicide, Vertisan Fungicide, Treoris Fungicide and DPX-LEM17 50WG Fungicide to address the potential risks identified in this assessment are as follows:

Key Risk-Reduction Measures

Human Health

As users may come into direct contact with penthiopyrad on the skin or through inhalation of spray mists, anyone mixing, loading and applying Fontelis Fungicide, Vertisan Fungicide, Treoris Fungicide and DPX-LEM17 50WG Fungicide must wear a long-sleeved shirt, long pants, shoes, socks and chemical resistant gloves, and users mixing/loading Vertisan Fungicide must also wear goggles or a face shield. For products that may be applied by aerial application equipment, pilots are not allowed to mix chemicals to be loaded onto the aircraft and the field crew and the mixer/loaders must wear chemical-resistant gloves, coveralls and goggles or face shield during mixing/loading. In addition, standard label statements to protect against drift during application were added to the label, and entry into treated areas is restricted for three days before performing detasseling activities on corn, for 12 hours after application for all other agricultural postapplication activities, and until sprays have dried for entering treated turf.

Environment

Label statements and no-spray buffer zones to mitigate the risk of spray drift to aquatic ecosystems are required. As well, label statements to identify sensitive components and mitigation measures to help reduce contamination of aquatic habitats are required.

Other Information

The relevant test data on which the decision is based (as referenced in PRD2011-26, *Penthiopyrad)* are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

Any person may file a notice of objection[5] regarding this registration decision within 60 days from the date of publication of this Registration Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides and Pest Management portion of the Health Canada's website (Request a Reconsideration of Decision, www.hc-sc.gc.ca/cps-spc/pest/part/protect-proteger/publi-regist/index-eng.php#rrd) or contact the PMRA's Pest Management Information Service.

[5] As per subsection 35(1) of the *Pest Control Products Act*.

Appendix I Comments and Responses

Comment:

Amendment of the supported level of control for sclerotinia stem rot on canola

The applicant, E. I. DuPont Canada Company, believes that the claim for sclerotinia stem rot on canola should be registered as control rather than suppression. The level of control observed in the submitted efficacy trials was comparable to the registered commercial standards with control claims for this pest. The applicant stated that the lower than expected levels of disease reduction could be explained by the conditions imposed on small plot trials where pathogen growth and multiple infection cycles are favoured, leading to disease levels higher than what would be expected under commercial production conditions. In addition, the crop could be infected at later stages, which further contributes to a perceived lower level of control at the end of the season. The applicant indicated that disease reduction levels in the trials are consistent with the expected level of control in the canola industry. The applicant provided information from canola experts, which stated that the levels of control obtained in the efficacy trials for Vertisan Fungicide and the commercial standards are typical of what would be expected in canola production. It was also stated that disease control in the area of 80% is rare and will result only if a fungicide application is made close to an infection event characterized by optimum environmental conditions and the presence of inoculum and provided that re-infection of the crop does not occur.

Response:

Twelve trials with moderate-to-high disease incidence and low-to-high disease severity were submitted and reviewed to support the claim. In the trials, Vertisan Fungicide provided an average of 46.2% (range: 11–66%) reduction in disease severity when disease pressure was moderate to high relative to the untreated check. The commercial standards, registered for control of this disease, were shown to provide an average of 37.7% (range: 7–60%) and 43.8% (range: 2–65%) control of disease severity in the same trials. The performance of the commercial standards, while lower than expected was comparable to Vertisan Fungicide. Yield data were also considered, although the increases observed were not significantly different from the control. Based on these results, it was difficult to conclude that the disease was being controlled. The weight of evidence suggested that Vertisan Fungicide was suppressing the disease.

The PMRA recognizes that many challenges could develop during field testing of fungicides and that several factors can affect trial results. However, if products perform below expectations, an explanation addressing these should be included in the value report. New information from the applicant provided an explanation for the level of efficacy expressed in the submitted trials by the commercial standards with respect to the higher disease pressure in small plot trials compared to the conditions observed in commercial canola production. Canola experts have also confirmed the goals and expectations of canola growers resulting from fungicide application for sclerotinia stem rot control. Information on the commercially acceptable level of control is essential in the review of proposed label claims and allows the PMRA to place the results of the efficacy trials in a broader context. Based on the additional information provided by the applicant, the PMRA agrees to amend the claim for sclerotinia stem rot (*Sclerotinia sclerotiorum*) from suppression to control. The use pattern supported by the PMRA remains the same. The claim for sclerotinia stem rot on canola indicated under Table 28 in PRD2011-26, *Penthiopyrad* will be amended to "control".